

PATENT COOPERATION TREATY

27 SEP 2004

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

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NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)

09 FEB 2004

AWP

Date of mailing
(day/month/year)

05.02.2004

Applicant's or agent's file reference
AXP/PG4790

IMPORTANT NOTIFICATION

International application No.
PCT/EP 03/03338

International filing date (day/month/year)
27.03.2003

Priority date (day/month/year)
28.03.2002

Applicant
GLAXO GROUP LIMITED

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international
preliminary examining authority:



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Authorized Officer

Geier, A

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference AXP/PG4790	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA416)	
International application No. PCT/EP 03/03338	International filing date (<i>day/month/year</i>) 27.03.2003	Priority date (<i>day/month/year</i>) 28.03.2002
International Patent Classification (IPC) or both national classification and IPC C07D265/30		
Applicant GLAXO GROUP LIMITED		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

I ☒ Basis of the opinion

II ☐ Priority

III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

IV ☐ Lack of unity of invention

V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

VI ☐ Certain documents cited

VII ☐ Certain defects in the international application

VIII ☐ Certain observations on the international application

Date of submission of the demand 30.09.2003	Date of completion of this report 05.02.2004
Name and mailing address of the international preliminary examining authority: <div style="display: flex; align-items: center;"> <div> European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840 </div> </div>	Authorized Officer Hass, C Telephone No. +49 30 25901-340



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/03338**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-20 as originally filed

Claims, Numbers

1-12 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/03338**

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 4 (with regard to industrial applicability)

because:

☒ the said international application, or the said claims Nos. 4 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-8, 10-20
	No: Claims	9
Inventive step (IS)	Yes: Claims	1-8, 10-20
	No: Claims	9
Industrial applicability (IA)	Yes: Claims	1-3, 5-20
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 4 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Cited documents

- D1: WO 98 56771 A (SCHERING AG) 17 December 1998 (1998-12-17) cited in the application
- D2: SARTORI E ET AL: 'SYNTHESIS AND ACTIVITIES OF NET ARYLSULFONAMIDO THROMBOXANE A2 RECEPTOR ANTAGONISTS' EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, FR, vol. 28, no. 7/8, 1993, pages 625-632, XP000396678 ISSN: 0223-5234 cited in the application
- D3: WO 95 31431 A (NISSHIN FLOUR MILLING CO; KIKUCHI HARUHIKO (JP); SATOH HIROAKI (JP) 23 November 1995 (1995-11-23)
- D4: EP-A-0 243 959 (DAINIPPON PHARMACEUTICAL CO) 4 November 1987 (1987-11-04)
- D5: WO 95 31442 A (NISSHIN FLOUR MILLING CO; KIKUCHI HARUHIKO (JP); SATOH HIROAKI (JP) 23 November 1995 (1995-11-23)

2. Novelty

2.1 The subject-matter of claim 9 is not novel in view of D2, page 631, left-hand column, line 17 ("methyl 3-aminomethyl benzoate").

2.2 The subject-matter of claims 1-8 and 10-12 is novel with regard to D1-D5:
The D1 compounds have no morpholine ring.

The D3 compounds similar to those of claims 1, 6 and 7 have no "free" urea group (D3, pages 28 and 35). The compound disclosed on page 41, line 5 of D3 does not have a ring on the "left-hand side" of the molecule.

The compound disclosed in D4, page 43, example 24 has an amide group as linking group.

The compound disclosed in D5, page 40, lines 6-10, is different from the compounds claimed in claims 11 and 12 at least because it has no A-corresponding group.

3. Inventive step

3.1 According to the description, the problem underlying the present application is to provide further compounds which are useful as pharmaceuticals, especially for the treatment of inflammation.

3.2 For the subject-matter of claim 1, D1 is the closest prior art since it also discloses compounds which have anti-inflammatory activity. However, the D1 compounds are piperazine derivatives, and they do not have a urea group. The present compound of claim 1 thus could not be deduced from D1. Therefore it can be said that the problem as defined above has been solved in a non-obvious way. For the subject-matter of product claim 1, process claim 2, pharmaceutical claims 3 to 5 and of claims 6 to 8 and 10 to 12, which are directed to intermediates (claim 9 is not novel, see above), inventive step can be acknowledged.

4. Industrial applicability

4.1 The subject-matter of claims 1-3 and 5-12 is industrially applicable.

4.2 For the assessment of the present claim 4 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

INTERNATIONAL SEARCH REPORT

27 SEP 2004

International Application No

PCT/EP 03/03338

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D265/30 C07C229/60 C07C215/18 A61K31/5375 A61P29/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98 56771 A (SCHERING AG) 17 December 1998 (1998-12-17) cited in the application claims 1,31-34 ---	1,3-5
X	SARTORI E ET AL: "SYNTHESIS AND ACTIVITIES OF NET ARYLSULFONAMIDO THROMBOXANE A2 RECEPTOR ANTAGONISTS" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, FR, vol. 28, no. 7/8, 1993, pages 625-632, XP000396678 ISSN: 0223-5234 cited in the application page 631, left-hand column, line 17: "methyl 3-aminomethyl benzoate" --- -/--	9

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

6 October 2003

Date of mailing of the international search report

15/10/2003

Name and mailing address of the ISA

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Authorized officer

Hass, C

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/03338

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WO 95 31431 A (NISSHIN FLOUR MILLING CO; KIKUCHI HARUHIKO (JP); SATOH HIROAKI (JP) 23 November 1995 (1995-11-23) page 28, line 21 - line 24 page 35, line 20 - line 23 page 41, line 5</p> <p style="text-align: center;">---</p>	1,2,6-8, 10
A	<p>EP 0 243 959 A (DAINIPPON PHARMACEUTICAL CO) 4 November 1987 (1987-11-04) page 43, example 24</p> <p style="text-align: center;">---</p>	1,10
A	<p>WO 95 31442 A (NISSHIN FLOUR MILLING CO; KIKUCHI HARUHIKO (JP); SATOH HIROAKI (JP) 23 November 1995 (1995-11-23) page 40, line 6 - line 10 page 42, line 2 - line 4 page 43, line 5</p> <p style="text-align: center;">---</p>	10-12
A,P	<p>WO 02 26723 A (HARRISON LEE ANDREW; JUDD DUNCAN BRUCE (GB); GLAXO GROUP LTD (GB);) 4 April 2002 (2002-04-04) claims 1,11,12,14,17-23,25,26; examples</p> <p style="text-align: center;">-----</p>	1-8,10

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/03338

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 4 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/03338

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9856771	A	17-12-1998	US 6207665 B1	27-03-2001
			AT 232522 T	15-02-2003
			AU 735462 B2	12-07-2001
			AU 8625898 A	30-12-1998
			DE 69811363 D1	20-03-2003
			DK 988292 T3	22-04-2003
			EE 9900565 A	15-06-2000
			EE 200200682 A	15-04-2003
			EE 200200683 A	15-04-2003
			EE 200200684 A	15-04-2003
			WO 9856771 A2	17-12-1998
			EP 1254899 A2	06-11-2002
			EP 0988292 A2	29-03-2000
			ES 2191320 T3	01-09-2003
			HU 0003929 A2	28-05-2001
			JP 2002503239 T	29-01-2002
			NO 996068 A	11-02-2000
			NO 20031373 A	11-02-2000
			PL 337758 A1	11-09-2000
			SK 171399 A3	12-09-2000
			TR 9903034 T2	21-06-2000
			US 2003158205 A1	21-08-2003
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			US 2002177598 A1	28-11-2002
WO 9531431	A	23-11-1995	BR 9507892 A	18-11-1997
			CA 2189964 A1	23-11-1995
			DE 69527786 D1	19-09-2002
			DE 69527786 T2	10-04-2003
			EP 0760362 A1	05-03-1997
			WO 9531431 A1	23-11-1995
			US 5753654 A	19-05-1998
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			AU 592177 B2	04-01-1990
			AU 7227587 A	05-11-1987
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			CZ 8702897 A3	11-11-1998
			DD 256325 A5	04-05-1988
			DE 3781195 D1	24-09-1992
			DE 3781195 T2	18-02-1993
			DK 218787 A	31-10-1987
			EP 0243959 A1	04-11-1987
			ES 2043617 T3	01-01-1994
			FI 871828 A ,B,	31-10-1987
			GR 3005934 T3	07-06-1993
			HK 18194 A	11-03-1994
			HU 45514 A2	28-07-1988
			HU 198193 B	28-08-1989
			JP 1686407 C	11-08-1992
			JP 3054937 B	21-08-1991
			JP 63264467 A	01-11-1988
			JP 2042069 A	13-02-1990
			MX 6263 A	01-11-1993
			NZ 220120 A	28-06-1989

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/03338

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0243959	A	PH 24049 A SG 494 G SK 289787 A3 SU 1597101 A3 US 4870074 A ZA 8703022 A KR 9508530 B1	05-03-1990 15-04-1994 03-06-1998 30-09-1990 26-09-1989 20-10-1987 31-07-1995
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WO 0226723	A 04-04-2002	AU 9014601 A BR 0114321 A CA 2423305 A1 CZ 20031194 A3 EP 1324991 A1 WO 0226723 A1 NO 20031443 A	08-04-2002 01-07-2003 04-04-2002 13-08-2003 09-07-2003 04-04-2002 26-05-2003